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Hippocampal dosimetry predicts the change in neurocognitive functions after whole brain radiotherapy

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Purpose or Objective: Whole brain radiotherapy (WBRT) has been the treatment of choice for patients with brain metastases. However, change/decline of neurocognitive functions (NCFs) resulting from impaired hippocampal neurogenesis might occur after WBRT. It is reported that hippocampal sparing would provide the preservation of NCFs. Our study aims to investigate the correlations between hippocampal dosimetry and neurocognitive outcomes in patients receiving hippocampal sparing during WBRT (HS-WBRT).

Material and Methods: Fifty prospectively recruited cancer patients underwent HS-WBRT for therapeutic or prophylactic purposes. Before receiving HS-WBRT, all participants received a battery of baseline neurocognitive assessment, including memory, executive functions and psychomotor speed. The follow-up neurocognitive assessment at 4 months after HS-WBRT was also performed. To deliver HS-WBRT, Volumetric Modulated Arc Therapy (VMAT) with two full arcs and two non-coplanar partial arcs was employed. For each treatment planning, dose volume histograms were generated for left hippocampus, right hippocampus, and the composite hippocampal structure respectively. Biologically equivalent doses in 2-Gy fractions (EQD2) assuming an alpha/beta ratio of 2 Gy were computed. To perform analyses addressing the correlation between hippocampal dosimetry and the change in NCF scores, pre- and post-HS-WBRT neurocognitive assessments were available in 32 patients.

Results: NCF scores were quite stable before and after HS-WBRT regarding hippocampus-dependent memory. For verbal memory, the corresponding EQD2 values of 0%, 10%, 50%, 80% irradiating the composite hippocampal structure with <12.60Gy, <8.81Gy, <7.45Gy and <5.83Gy respectively were significantly associated with neurocognitive preservation indicated by the immediate recall of Word List Test of Wechsler Memory Scale-III. According to logistic regression analyses, it showed that dosimetric parameters specific to left hippocampus exerted an influence on immediate recall of verbal memory (adjusted odds ratio, 4.08; *p*-value, 0.042, predicting patients' neurocognitive decline after HS-WBRT).

Conclusion: Functional preservation by hippocampal sparing during WBRT is indeed achieved in our study. Providing that modern VMAT techniques can reduce the dose irradiating bilateral hippocampi below dosimetric threshold, patients should be recruited in prospective trials of hippocampal sparing during cranial irradiation to accomplish neurocognitive preservation while maintaining intracranial control.

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Post-radiation neuronal depletion in hippocampus measured by in-vivo magnetic resonance spectroscopy

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Purpose or Objective: Ongoing clinical trials are evaluating advantage of hippocampal avoiding whole brain radiotherapy (WBRT), however, further basic research focusing on in-vivo description of radiation injury processes is still needed. Using magnetic resonance spectroscopy (MRS), it is possible to measure specific metabolite concentrations in any region of interest in the brain. N-acetylaspartate (NAA) represents a marker of viable neurons. To describe hypothesized post-WBRT neuronal depletion in hippocampus, we prospectively measured changes in NAA concentrations 4 months after WBRT.

Material and Methods: Patients referred for WBRT with favorable prognosis estimated by graded prognostic assessment and without MRI hippocampal pathology were eligible for study enrollment. Before standard WBRT (two-dimensional planning, 2 laterolateral 6 megavoltage fields, dose 10x3.0 Gy delivered by linear accelerator), hippocampal spectroscopy was performed using GE Medical Systems Discovery MR 750 3T. Region of interest was placed through the whole temporal lobi with the voxel layer position adjusted based on the localization of hippocampi. Specialized software was utilized for measurement of absolute NAA concentration in voxels within right, left and both hippocampi. The controle MRS with the same setup parameters was performed 4 months after the end of course of WBRT. Wilcoxon's signed rank test was employed for calculation of NAA concentration changes.

Results: Thirty-five patients (68% mens, mean age 59.5) were enrolled and underwent baseline MRS while only 18 (51%) of them finished the whole protocol with control measurement (15 died before and 2 refused). The most common primary cancer was lung (44%), kidney (20%) and breast (15%). On average, 9 voxels were analyzed per right and left hippocampus. The mean NAA concentration pre- and post-WBRT was 8.47 [mM] and 7.43 [mM] for the right and 8.80 [mM] and 8.04 [mM] for the left hippocampus, respectively. The statistically significant decrease was observed in the right (-11.4%; 95% confidence interval -6.9 to -15.9; p=0.0003) as well as in the left (-8.5%; 95% confidence interval -2.9 to -14.0; p=0.0034) hippocampus.

Conclusion: Hippocampal MR spectroscopy is feasible and sensitive method for non-invasive measurement of brain radio injury. In our study, we observed correlation between left hippocampal N-acetylaspartate concentration and verbal memory decline with smaller effect of right hippocampus. Robust analysis of pre-irradiation imaging studies may provide valuable predictive biomarkers for decision making for the best radiotherapy approach in the treatment of brain metastases.

Proffered Papers: Brachytherapy 4: Gynae-Breast

OC-0351

MRI-guided brachytherapy in cervical cancer: high doses to small bowel don't predict late morbidity

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Purpose or Objective: To establish dose-volume effect correlations for late small bowel toxicities in patients treated for locally advanced cervical cancer with concomitant chemoradiation followed by MRI-guided adaptive brachytherapy.

Material and Methods: In a cohort of patients treated in curative intent and followed prospectively, those who had completed the treatment one year before were retained for this study. The small bowel loops were delineated during the planning process, but no specific dose constraint was applied. The dosimetric data, converted in 2 Gy equivalent ($\alpha/\beta=3$) were confronted to the occurrence of small bowel events: diarrhea, pain, flatulence, bleeding, obstruction, and fistula. Patients were followed every 3 months for the first year then every 6 months, for 3 years, then annually. Late morbidity was defined over the threshold of 90 days from treatment initiation and assessed using the CTC-AE 3.0. Patients who experienced recurrences were censored from the date of their relapse. Dose-effect relationships were assessed using